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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,740	09/18/2000	Wolfgang Wuttke	WINTE-045244	5915

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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/15/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/646,740	Wuttke et al.
Examiner	**Art Unit**
Michele Flood	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 27, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-25* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4,8*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendments filed on August 27, 2001. Acknowledgment is made of Applicant's cancellation of Claims 1-16, and newly submitted Claims 17-25.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 19-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect comprising administering to the patient an effective amount of *Belamcanda sinensis*, does not reasonably provide enablement for a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect comprising administering to the patient an effective amount of a medicament comprising an extract from any and all plants of the family Iridaceae. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method of producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the

patient an effective amount of a medicament comprising an extract from Iridaceae, with the proviso that *Belamcanda chinensis* extract is not used for treating peri-menopausal and post-menopausal disorders. The claims are further drawn to method, wherein the extract comprises at least one of tectorigenin and tectorigenin glycoside. The claims are further drawn to method, wherein the extract is enriched with at least one of tectorigenin and tectorigenin glycoside. The claims are further drawn to method, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of a cardiovascular disease. The claims are further drawn to method, wherein the cardiovascular disease is atherosclerosis. The claims are further drawn to method, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of osteoporosis. The claims are further drawn to method, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of a climacteric disorder. The claims are further drawn to method, wherein the production of the estrogen-type effect comprises preventing or alleviating hot flushes.

The specification broadly discloses a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect comprising the administration of extracts from Iridaceae, and tectorigenin and/or tectorigenin glycosides as a medicament. While the specification does demonstrate an *in vitro* method and an *in vivo* method for producing an estrogen-type effect in an ovariectomized rat (a recognized model for the post-menopausal woman in whom the endogenous estradiol production has subsided) comprising the single or repeated administration (i.e., organic solvents or with supercritical carbon dioxide*) Belamcanda*

sinensis
~~*chinensis*~~ extract, wherein the claimed functional effect resulted in the lowering of serum LH levels, an inhibition of the GnRH pulse generator in hypothalamic estrogen-receptive structures, and inhibition of hyophysary LH secretion and similar functional effects comprising the administration of tectorigenin to ovariectomized rats, the specification does not disclose a method for producing an estrogen-type in patient without causing a substantial effect comprising the administration of an effective amount of a medicament comprising an extract from any and all plants from the family Iridaceae. There is no guidance in the specification, other than the aforementioned examples directed to the delivery of either an extract of *Belamcanda* *sinensis* ~~*chinensis*~~ or tectorigenin to ovariectomized rats. In order to enable the skilled artisan to practice the invention as claimed, Applicant would have to demonstrate the functional effect and describe the therapeutic effective amounts of extract intended for a therapeutic treatment for the claimed disease conditions. Moreover, as the claims are drawn to a method of administering pharmaceutically acceptable compositions which would in effect 'prevent' the various disease conditions from happening, they would require supporting evidence which clearly define the ingredients or constituents therein and supporting evidence because of the unpredictability in biological responses to therapeutic treatments or therapeutic prophylaxis. In order to enable the skilled artisan to practice the invention as claimed, Applicant would have to demonstrate the functional effect and describe the therapeutic effect or prophylactic effect, and describe the effective amounts of each ingredient for the administration of the composition intended for a therapeutic treatment or prophylaxis. Moreover, the instant application does not provide a

working example providing data which shows that the composition of the instant claims would indeed prevent an event such as the claimed designated disease conditions. Thus, Applicant has not demonstrated the claimed functional effect of preventing and treating each and every of the claimed disease conditions comprising the administration of any and all plant extracts from the family Iridaceae. Other than the demonstrated administration of the claimed medicaments comprising either an extract of *Belamcanda sinensis* and tectorigenin, Applicant has not demonstrated a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect method, said method comprising administering to a patient an effective amount of any and all plant extracts from the family Iridaceae, with the proviso that *Belamcanda sinensis* extract is not used for treating peri-menopausal and post-menopausal disorders. Furthermore, it is noted that the specification is particularly silent as to which organic solvents are used in the making of the *Belamcanda sinensis* extract or from which plant source, if any plant source at all, the tectorigenin is obtained. Accordingly, it would take undue experimentation without a reasonable expectation of success as to how to determine which plants of the family Iridaceae could be used to make the claim designated plant extract, how to determine the solvents used in the making of any and all of the claim designated plant extracts of the family Iridaceae, how to determine the plant parts used in the making of the claimed designated plant extracts of the family Iridaceae, and how to determine the effective therapeutic amounts of any and all of the claim designated plant extracts of the family Iridaceae which would

have the claimed functional therapeutic effect in the treatment and/or prophylaxis of the claimed disease conditions, as broadly claimed by Applicant.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-20 are rendered vague and indefinite by the term "extract" because this term, in and of itself, does not adequately delineate its metes and bounds. This term is best defined as a product-by-process since product-by-process claims are intended to define products which are otherwise difficult to define (and/or distinguish from the prior art). For example, is the extract obtained via extraction with water, a polar solvent, a non-polar solvent, an acid or base, a squeezed extract, or something else? In addition, from what part(s) of the plant is the extract obtained? It is well accepted in the herbal art that extraction with one of various distinct solvents, as well as from particular parts of therapeutic plants, has a profound impact on the final product with respect to the presence, absence, amounts, and/or ratios of active ingredients therein and, thus, its ability to provide the desired functional effect(s) instantly claimed and/or disclosed. Since the extract itself is clearly essential to the claimed invention, the step(s) by which the

claimed extract is obtained are also clearly essential and, therefore, must be recited in the claim language itself (i.e., as a product-by-process). Please note that although the claims are interpreted in light of the specification, critical limitations from the specification cannot be read into the claims (see, e.g., *In re* Van Glens, 988 F.2d 1181, 26 PSPG2d 1057 (Ded. Cir. 1991)). Accordingly, without the recitation of all these critical limitations as set forth above, the claims do not adequately define the instant invention.

With regard to Claims 17 and 18, there is an apparent misspelling of the term "Belamcandra chinesis". Applicant may overcome the rejection by replacing "Belamcandra chinesis" with "*Belamcandra chinensis*".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-18 and 24 are rejected under 35 U.S.C. 102(a) as being anticipated by Li (N) or Ning (O).

Applicant claims a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an

effective amount of a medicament comprising an extract from Iridaceae, with the proviso that "*Belamcanda chinensis*" extract is not used for treating peri-menopausal and post-menopausal disorders. Applicant further claims a method according to claim 17, wherein the extract is a *Belamcanda chinensis* extract. Applicant further claims a method according to claim 17, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of a climacteric disorder.

Li teaches a traditional Chinese medicine for resisting cancer and inhibiting tumor, comprising the administration of a medicament comprising bushy sophora root, hedyotis, bearded scutellaria, belamcanda root, scutellaria root, prunella, forsythia fruit, lonicera flower and Zhejiang fritillaria bulb as main medicinal ingredients and adopts the following processes of decoction, filtering, precipitation of aqueous extract by adding ethyl alcohol, centrifugal clarification of liquid medicine and recovering ethyl alcohol. The medicament taught by Li kills cancer cells, and can reduces tumor up to 59.3%, and its effective rate is up to 90%.

Ning teaches a Chinese patent medicine for treating and prophylaxis of ovarian cancer with high effective rate up to 87.6% and no toxic by-effect, wherein the medicament comprises forsythia fruit, scrophularia root, belamcanda rhizome, burreed tuber, zedoary, etc.

As cancer and ovarian cancer are considered climacteric disorders, the references of Li and Ning anticipate the claimed subject matter.

Claims 17, 21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Breton et al. (P).

Applicant claims a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an effective amount of a medicament comprising an extract from Iridaceae, with the proviso that *Belamcanda chinensis* extract is not used for treating peri-menopausal and post-menopausal disorders. Applicant further claims a method according to claim 17, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of a cardiovascular disease. Applicant further claims a method according to claim 17, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of a climacteric disorder.

Breton teaches a method for treating cardiovascular diseases comprising the administration of an effective amount of a medicament comprising an extract of a plant from the Iridaceae family. The pharmaceutical compositions taught by Breton are also used in the treatment of disorders associated with overproduction or excessive secretion of substance P, such as CNS disorders, respiratory disorders, allergies, inflammation, pain, gastrointestinal disorders, skin disorders, fibrosis, collagen maturation disorders, cardiovascular disorders, vasospasm, immunological disorders and/or disorders of the urinary tract; for treating sensitive skin; for preventing and/or combating skin and/or mucosal irritation.

The reference anticipates the claimed subject matter.

Claims 17 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Soma et al. (A).

Applicant claims a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an effective amount of a medicament comprising an extract from Iridaceae, with the proviso that "*Belamcanda chinensis*" extract is not used for treating peri-menopausal and post-menopausal disorders. Applicant further claims a method according to claim 17, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of osteoporosis.

Soma teaches a method for the administration of a glycolipid extract from plants of the Iridaceae family, which is effective in stimulating the immune system of an animal to effect at least one of osteogenesis, oviposition, and shell strength improvement. The reference anticipates the claimed subject matter.

Claims 17 and 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Bliadze et al. (Q).

Applicant claims a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an effective amount of a medicament comprising an extract from Iridaceae, with the proviso that "*Belamcanda chinensis*" extract is not used for treating peri-menopausal and post-menopausal disorders. Applicant further claims a method according to claim 17, wherein the production of

the estrogen-type effect comprises treatment and/or prophylaxis of a cardiovascular disease, and wherein the cardiovascular disease is atherosclerosis.

Bliadze teaches the administration of tonic drink comprising iris root, which reduces the brittleness of blood vessels, thus preventing arteriosclerosis. The reference anticipates the claimed subject matter.

Claims 17 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 07138179A (R) or Liu et al. (S).

Applicant claims a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an effective amount of a medicament comprising an extract from Iridaceae, with the proviso that "*Belamcanda chinensis*" extract is not used for treating peri-menopausal and post-menopausal disorders. Applicant further claims a method according to claim 17, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of a climacteric disorder.

JP 07138179A teaches the administration of a medicament comprising an extract of *Belamcanda chinensis*, which prevents skin ageing. As skin-ageing is known in the art as a climacteric disorder, the reference anticipates the claimed subject matter.

Liu teaches the administration of an oral contraceptive comprising an extract of sweet iris flower. Liu teaches that the administration of the drug is without side effects and that

contraceptive time is controlled by the time of taking the contraceptive. As lack of birth control, is indicative of climacteric disorder, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-20 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Esaki (U) and Petrie et al. (B) in view of Shawl (V) and Zhou et al. (W).

Applicant claims a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, the method comprising administering to the patient an effective amount of a medicament comprising an extract from Iridaceae, with the proviso that is not used for treating peri-menopausal and post-menopausal disorders. Applicant further claims a method according to claim 17, wherein the extract is *Belamcanda chinensis* extract. Applicant further claims a method according to claim 17, wherein the extract comprises at least one of tectorigenin and tectorigenin glycoside. Applicant further claims a method according to claim 17, wherein the extract is enriched with at least one of tectorigenin and tectorigenin glycoside. Applicant further claims a method according to claim 17, wherein the production of the estrogen-type effect comprises treatment and/or prophylaxis of osteoporosis.

Esaki teaches that the administration of tectoridin (a tectorigenin glycoside) and tectorigenin to the rat causing a weak estrogenlike action. In Column 4, lines 46-65, Petrie teaches the administration of representative compounds for the treatment and prophylaxis of various disease conditions, including age-related osteoporosis. See Column 21, lines 58-61, wherein Petrie teaches the use of tectorigenin in the referenced method.

The teachings of Esaki and Petrie are set forth above. Neither Esaki nor Petrie teach a method for producing an estrogen-type in a patient comprising the administration of a medicament comprising an extract of Iridaceae. However, it would have been obvious to one of ordinary skill in the art to provide the claimed method because at the time the invention was made it was well known in the art that tectorigenin and tectorigenin glycoside could be obtained from a plant belonging to the family Iridaceae, as evidenced from the teachings of Shawl and Zhou. For instance, Shawl teaches that both tectoridin and tectorigenin can be isolated from *Iris crocea* and Zhou teaches that both tectoridin and tectorigenin can be isolated from an ethanolic extract of the roots of *Belamcanda chinensis*. At the time the invention was made, one of ordinary skill in the art would have been motivated to provide a method for producing an estrogen-type effect in a patient without causing a substantial uterotrophic effect, said method comprising the administering to a patient an effective amount of a medicament comprising an extract of Iridaceae, wherein the extract either comprised or was enriched with at least one of tectorigenin and tectorigenin glycoside because both Shawl and Zhou teach plant extracts of the family Iridaceae which comprise tectorigenin and tectorigenin. One of ordinary skill in the art at

the time the invention was made would have had a reasonable expectation of success to administer the claim designated plant extracts to provide the claimed functional effect and therapeutic effect for treatment and prophylaxis of various disease conditions, wherein the plant extracts either comprised or was enriched with at least one of tectorigenin and tectorigenin glycoside because Esaki shows administering tectorigenin and tectoridin has estrogenlike action with low toxicity and Petrie teaches that the administering of compounds of the general structure of tectorigenin are effective in the treatment and prophylaxis of osteoporosis, age-related osteoporosis, post-menopausal osteoporosis, wound healing or tissue repair, elevation of peak bone mass in pre-menopausal women, arthritis, etc.

With regard to Claims 21-22 and 24-25, one of ordinary skill in the art would have been motivated to administer a plant extract from the family Iridaceae, plant extract either comprised or was enriched with at least one of tectorigenin and tectorigenin glycoside because Petrie teaches an *in vivo* method for the administration of his compounds to ovariectomized animals, wherein the claimed functional effect of producing an estrogen-type effect with minimal uterotrophic effect is demonstrated (see Column 10, lines 51-67 to Column 11, lines 1-13). As it was well known in the art at the time the invention was made that ovariectomized animals are a model for the for the post-menopausal woman in whom the endogenous estradiol production has subsided, one of ordinary skill in the art would have had a reasonable expectation of success that the administering of the claim designated plant extracts from the family Iridaceae, wherein the plant extract comprised or was enriched with at least one of tectorigenin and tectorigenin

glycoside would have the claimed functional effect for being effective in each of the claim designated disease conditions because each of the claim designated disease conditions were associated with the menopausal woman.

As each of the references indicate that the various proportions and amounts of the ingredients used in the claimed composition or the claimed composition/pharmaceutical combinations are result variables, they would have been routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by each of the references.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is (703) 308-9432. The examiner can normally be reached on Monday through Friday from 7:15 am to 3:45 pm. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196 or the Supervisory Patent Examiner, Michael Wityshyn whose telephone number is (703) 308-4743.

MCF

November 5, 2001

CHRISTOPHER R. TATE
PRIMARY EXAMINER